Attach Paper # 15

EAST: DERWENT EPO JPO USPAT 09/227,687 03/09/01

| | | | |
|---|---|---|---|
| BRS | L5 | 309 | 424/93.1.icls. |
| BRS | L6 | 408 | 424/93.2.icls. |
| BRS | L7 | 336 | 424/93.21.icls. |
| BRS | L8 | 0 | 424/93.93.4.icls. |
| BRS | L9 | 160 | 424/93.4.icls. |
| BRS | L10 | 0 | 93.42.icls. |
| BRS | L12 | 288 | 424/234.1.icls. |
| BRS | L13 | 35 | 424/237.1.icls. |
| BRS | L11 | 4 | 424/93.42.icls. |
| BRS | L14 | 0 | 11 and gene |
| BRS | L15 | 1224 | 5 or 6 or 7 or 9 or 11 or 12 or 13 |
| BRS | L16 | 909 | 15 and gene |
| BRS | L17 | 789 | 16 and recombinant |
| BRS | L18 | 406 | 15 and (gene with transform$) |
| BRS | L19 | 147 | 18 and pathogen |
| BRS | L20 | 402 | 18 and (screen$ or identif$ or isolat$) |
| BRS | L21 | 314 | 18 and ((screen$ or identif$ or isolat$) with gene) |
| BRS | L22 | 2 | 5,981,182.pn. |
| BRS | L23 | 14 | 5801013.pn. 5871987.pn. 5885815.pn. 6174713.pn. 5656470.pn. 5798240.pn. |
| BRS | L24 | 12 | tally-f$.in. |
| BRS | L25 | 119 | tao-j$.in. |
| BRS | L26 | 32 | wendler-p$.in. |
| BRS | L27 | 11 | connelly-g$.in. |
| BRS | L28 | 78 | gallant-d$.in. |
| BRS | L29 | 0 | 24 and 25 and 26 and 27 and 28 |
| BRS | L30 | 248 | 24 or 25 or 26 or 27 or 28 |
| BRS | L31 | 6 | 30 and animal |
| BRS | L32 | 29 | 30 and (method with (determin$ or isolat$ or screen$ or identif$)) |
| BRS | L33 | 0 | 30 and pro3 |
| BRS | L34 | 0 | 30 and prors |
| BRS | L35 | 5 | 30 and aureus |
| BRS | L36 | 1308 | 514/44.icls. |
| BRS | L37 | 1112 | 36 and vivo |
| BRS | L38 | 469 | 37 and reporter |
| BRS | L39 | 120 | 38 and pathogen |
| BRS | L40 | 265 | 38 and ((transformed or recombinant) with cell) |
| BRS | L41 | 192 | 36 and ((ex adj2 vivo) and reporter) |
| BRS | L42 | 0 | 36 and ((ex adj2 vivo) with reporter) |
| BRS | L43 | 2 | 36 and ((ex adj2 vivo) with (lac or gfp or cat)) |
| BRS | L44 | 122 | 36 and ((ex adj2 vivo) and reporter) and (gfp or lac or cat) |
| BRS | L45 | 17 | 44 and tet |

+ Bujard-f.IN. + Tet

09/227,687
Attach Paper # 15

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      (FILE 'HOME' ENTERED AT 18:27:20 ON 09 MAR 2001)

      FILE 'MEDLINE, EMBASE, CAPLUS, BIOSIS' ENTERED AT 18:27:40 ON 09 MAR 2001
L1             485 S (TALLY, F?)/IN,AU
L2             855 S (TAO, J?)/IN,AU
L3              58 S (WENDLER, P?)/IN,AU
L4             108 S (CONNELLY, G?)/IN,AU
L5              72 S (GALLANT, C?)/IN,AU
L6             492 S (GALLANT, D?)/IN,AU
L7               0 S L1 AND L2 AND L3 AND L4 AND L6
L8            1977 S L1 OR L2 OR L3 OR L4 OR L6
L9              14 S L8 AND TET
L10              6 DUPLICATE REMOVE L9 (8 DUPLICATES REMOVED)
L11             15 S L8 AND (METHOD (S) (ISOLATION OR IDENTIFICATION OR SCREENING
L12             11 DUPLICATE REMOVE L11 (4 DUPLICATES REMOVED)
L13              0 S L8 AND PRO3
L14              0 S L8 AND PC3844
L15              0 S L8 AND PRORS
L16              1 S L8 AND (INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANI
L17            597 S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?))
AND
L18              0 S L17 AND TET
L19            126 S L17 AND INDUC?
L20             75 S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?))
AND
L21              0 S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?))
AND
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TERMINAL (ENTER 1, 2, 3, OR ?):2

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| NEWS | 3 | Oct 27 | New Extraction Code PAX now available in Derwent Files |
| NEWS | 4 | Oct 27 | SET ABBREVIATIONS and SET PLURALS extended in Derwent World Patents Index files |
| NEWS | 5 | Oct 27 | Patent Assignee Code Dictionary now available in Derwent Patent Files |
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| NEWS | 16 | Feb 06 | Engineering Information Encompass files have new names |
| NEWS | 17 | Feb 16 | TOXLINE no longer being updated |

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=> FILE MEDLINE EMBASE CAPLUS BIOSIS

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| FULL ESTIMATED COST | 0.15 | 0.15 |

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FILE 'BIOSIS' ENTERED AT 18:27:40 ON 09 MAR 2001
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=> S (TALLY, F?)/IN,AU

'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L1          485 (TALLY, F?)/IN,AU

=> S (TAO, J?)/IN,AU

'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L2          855 (TAO, J?)/IN,AU

=> S (WENDLER, P?)/IN,AU

'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L3           58 (WENDLER, P?)/IN,AU

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'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L4          108 (CONNELLY, G?)/IN,AU

=> S (GALLANT, C?)/IN,AU

'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L5           72 (GALLANT, C?)/IN,AU

=> S (GALLANT, D?)/IN,AU

'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L6          492 (GALLANT, D?)/IN,AU

=> D HIS


     (FILE 'HOME' ENTERED AT 18:27:20 ON 09 MAR 2001)

     FILE 'MEDLINE, EMBASE, CAPLUS, BIOSIS' ENTERED AT 18:27:40 ON 09 MAR 2001
L1           485 S (TALLY, F?)/IN,AU
L2           855 S (TAO, J?)/IN,AU
L3            58 S (WENDLER, P?)/IN,AU
L4           108 S (CONNELLY, G?)/IN,AU
L5            72 S (GALLANT, C?)/IN,AU
L6           492 S (GALLANT, D?)/IN,AU

=> S L1 AND L2 AND L3 AND L4 AND L6

L7             0 L1 AND L2 AND L3 AND L4 AND L6
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=> S L1 OR L2 OR L3 OR L4 OR L6

L8          1977 L1 OR L2 OR L3 OR L4 OR L6

=> S L8 AND TET

L9            14 L8 AND TET

=> DUPLICATE REMOVE L9

DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N

PROCESSING COMPLETED FOR L9
L10             6 DUPLICATE REMOVE L9 (8 DUPLICATES REMOVED)

=> D TI L10 1-6


L10  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2001 ACS
TI   Tetracycline-inducible gene expression in gram-positive bacteria such as
     Staphylococcus and Bacillus

L10  ANSWER 2 OF 6  MEDLINE                                  DUPLICATE 1
TI   Inhibition of protein synthesis occurring on tetracycline-resistant,
     TetM-protected ribosomes by a novel class of tetracyclines, the
     glycylcyclines.

L10  ANSWER 3 OF 6  MEDLINE                                  DUPLICATE 2
TI   Glycylcyclines. 1. A new generation of potent antibacterial agents
through
     modification of 9-aminotetracyclines.

L10  ANSWER 4 OF 6  MEDLINE                                  DUPLICATE 3
TI   In vitro and in vivo antibacterial activities of the glycylcyclines, a
new
     class of semisynthetic tetracyclines.

L10  ANSWER 5 OF 6  EMBASE  COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI   Characterization of pBFTM10, a clindamycin-erythromycin resistance
     transfer factor from Bacteroides fragilis.

L10  ANSWER 6 OF 6  CAPLUS  COPYRIGHT 2001 ACS
TI   Mechanisms of drug-resistance transfer in Bacteroides fragilis


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     FILE 'MEDLINE, EMBASE, CAPLUS, BIOSIS' ENTERED AT 18:27:40 ON 09 MAR 2001
L1           485 S (TALLY, F?)/IN,AU
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L4           108 S (CONNELLY, G?)/IN,AU
L5            72 S (GALLANT, C?)/IN,AU
L6           492 S (GALLANT, D?)/IN,AU
L7             0 S L1 AND L2 AND L3 AND L4 AND L6
L8          1977 S L1 OR L2 OR L3 OR L4 OR L6
L9            14 S L8 AND TET
L10            6 DUPLICATE REMOVE L9 (8 DUPLICATES REMOVED)

=> S L8 AND (METHOD (S) (ISOLATION OR IDENTIFICATION OR SCREENING OR
DETERMINING)
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UNMATCHED LEFT PARENTHESIS 'AND (METHOD'
The number of right parentheses in a query must be equal to the number of left parentheses.

=> S L8 AND (METHOD (S) (ISOLATION OR IDENTIFICATION OR SCREENING OR DETERMINING))

L11 15 L8 AND (METHOD (S) (ISOLATION OR IDENTIFICATION OR SCREENING OR DETERMINING))

=> DUPLICATE REMOVE L11

DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N

PROCESSING COMPLETED FOR L11
L12 11 DUPLICATE REMOVE L11 (4 DUPLICATES REMOVED)

=> D TI L12 1-11

L12 ANSWER 1 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
TI Enhancing drug discovery: Utilization of VITATM fluorescently labeled ligands in high throughput capillary electrophoresis screening.

L12 ANSWER 2 OF 11 MEDLINE DUPLICATE 1
TI Detection of small-molecule enzyme inhibitors with peptides isolated from phage-displayed combinatorial peptide libraries.

L12 ANSWER 3 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
TI Fungi for pitch reduction and their preparation.

L12 ANSWER 4 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
TI Platform assay development strategy: Active-site directed peptides as tools for HTS.

L12 ANSWER 5 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
TI Bacterial SecA as an antimicrobial target.

L12 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2001 ACS
TI Chemometric Labeling of Cereal Tissues in Multichannel Fluorescence Microscopy Images Using Discriminant Analysis

L12 ANSWER 7 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 2
TI Membrane transport properties of mammalian oocytes: A micropipette perfusion technique.

L12 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2001 ACS
TI Analysis of petroleum acids in Dushanzi distillate

L12 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2001 ACS
TI T4 radioimmunoassay of dried blood samples on filter paper and its clinical application

L12 ANSWER 10 OF 11 MEDLINE DUPLICATE 3
TI Differentiation of Bacteroides ovatus and Bacteroides thetaiotaomicron by means of bacteriophage.

L12 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
TI QUANTITATIVE ISOLATION OF RADIO LABELED METABOLITES WITHOUT CHROMATOGRAPHY
MEASUREMENTS OF THE BIOSYNTHESIS OF PURINES PYRIMIDINES AND UREA IN ISOLATED HEPATOCYTES.

=> D IBIB AB L12 1-4

L12 ANSWER 1 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:540761 BIOSIS
DOCUMENT NUMBER: PREV200000540761
TITLE: Enhancing drug discovery: Utilization of VITATM fluorescently labeled ligands in high throughput capillary electrophoresis screening.
AUTHOR(S): Finn, J. (1); Glicksman, M. (1); Riera, T. (1); Gallant, P.
(1); **Tao, J. (1)**; Chapple, J. (1); Dunayevskiy, Y.; Hughes, D.
CORPORATE SOURCE: (1) Cubist Pharmaceuticals, Inc., Cambridge, MA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 226. print. Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L12 ANSWER 2 OF 11 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000130935 MEDLINE
DOCUMENT NUMBER: 20130935
TITLE: Detection of small-molecule enzyme inhibitors with peptides isolated from phage-displayed combinatorial peptide libraries.
AUTHOR: Hyde-DeRuyscher R; Paige L A; Christensen D J; Hyde-DeRuyscher N; Lim A; Fredericks Z L; Kranz J; Gallant P; Zhang J; Rocklage S M; Fowlkes D M; **Wendler P A**; Hamilton P T
CORPORATE SOURCE: Novalon Pharmaceutical Corporation, Durham, NC 27703, USA.
SOURCE: CHEMISTRY AND BIOLOGY, (2000 Jan) 7 (1) 17-25. Journal code: CNA. ISSN: 1074-5521.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY WEEK: 20000503
AB BACKGROUND: The rapidly expanding list of pharmacologically important targets has highlighted the need for ways to discover new inhibitors that are independent of functional assays. We have utilized peptides to detect inhibitors of protein function. We hypothesized that most peptide ligands identified by phage display would bind to regions of biological interaction in target proteins and that these peptides could be used as sensitive probes for detecting low molecular weight inhibitors that bind to these sites. RESULTS: We selected a broad range of enzymes as targets for phage display and isolated a series of peptides that bound specifically to each target. Peptide ligands for each target contained similar amino acid sequences and competition analysis indicated that they bound one or two sites per target. Of 17 peptides tested, 13 were found to be specific inhibitors of enzyme function. Finally, we used two peptides specific for Haemophilus influenzae tyrosyl-tRNA synthetase to show that a simple binding assay can be used to detect small-molecule inhibitors with potencies in the micromolar to nanomolar range. CONCLUSIONS: Peptidic surrogate ligands identified using phage display are preferentially targeted to a limited number of sites that inhibit enzyme function. These peptides can be utilized in a binding assay as a rapid and sensitive **method** to detect small-molecule inhibitors of target protein

function. The binding assay can be used with a variety of detection systems and is readily adaptable to automation, making this platform ideal for high-throughput **screening** of compound libraries for drug discovery.

L12 ANSWER 3 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:279564 BIOSIS
DOCUMENT NUMBER: PREV200000279564
TITLE: Fungi for pitch reduction and their preparation.
AUTHOR(S): Farrell, Roberta L. (1); Hadar, Yitzhak; **Wendler, Philip A.**; Zimmerman, Wendy
CORPORATE SOURCE: (1) Watertown, MA USA
ASSIGNEE: Clariant Finance (BVI) Limited, Tortola, British Virgin Islands
PATENT INFORMATION: US 5998197 December 07, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 7, 1999) Vol. 1229, No. 1, pp. No pagination. e-file..
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Ascospores of wood-penetrating, pitch-grading fungi of the class of Ascomycotina and Deuteromycotina, eg. Ophiostromas, may be screened to provide fungi combining the properties of good growth on non-sterile wood substrates and minimized or even enhanced brightness effects for use in pitch reduction of wood substrates, eg. logs and wood chips. A new and improved method of isolating such ascospores involving effective suspension in an oil consumable by the fungus, eg. a vegetable oil, and then treatment of the oil with a dispersing agent is also disclosed.

L12 ANSWER 4 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:258890 BIOSIS
DOCUMENT NUMBER: PREV199900258890
TITLE: Platform assay development strategy: Active-site directed peptides as tools for HTS.
AUTHOR(S): **Wendler, P. (1)**; Gallant, P. (1); Kranz, J. (1); Lim, A. (1); Namchuk, M. (1); Zhang, J. (1); Rocklage, S. (1); Deruyscher; Paige, L.; Hyde-Deruyscher, N.; Hamilton, P.; Fredericks, Z.
CORPORATE SOURCE: (1) Cubist Pharmaceuticals, Inc., Cambridge, MA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1998) Vol. 38, pp. 274.
Meeting Info.: 38th Interscience Conference on Antimicrobial Agents and Chemotherapy San Diego, California, USA September 24-27, 1998 American Society for Microbiology
.
DOCUMENT TYPE: Conference
LANGUAGE: English

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FILE 'MEDLINE, EMBASE, CAPLUS, BIOSIS' ENTERED AT 18:27:40 ON 09 MAR 2001
L1 485 S (TALLY, F?)/IN,AU
L2 855 S (TAO, J?)/IN,AU
L3 58 S (WENDLER, P?)/IN,AU
L4 108 S (CONNELLY, G?)/IN,AU
L5 72 S (GALLANT, C?)/IN,AU
L6 492 S (GALLANT, D?)/IN,AU
L7 0 S L1 AND L2 AND L3 AND L4 AND L6
L8 1977 S L1 OR L2 OR L3 OR L4 OR L6

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L9            14 S L8 A[redacted] TET
L10            6 DUPLIC[redacted]E REMOVE L9 (8 DUPLICATES REMOV[redacted]
L11           15 S L8 AND (METHOD (S) (ISOLATION OR IDENTIFICATION OR SCREENING
L12           11 DUPLICATE REMOVE L11 (4 DUPLICATES REMOVED)

=> S L8 AND PRO3

L13            0 L8 AND PRO3

=> S L8 AND PC3844

L14            0 L8 AND PC3844

=> S L8 AND PRORS

L15            0 L8 AND PRORS

=> S L8 AND (INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANISM))

L16            1 L8 AND (INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANISM)
                 )

=> D IBIB AB L16

L16  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         1999:451420  CAPLUS
DOCUMENT NUMBER:          131:85158
TITLE:                    Method for identifying validated target and assay
                          combinations
INVENTOR(S):              Tally, Francis P.; Tao, Jianshi; Wendler,
                          Philip A.; Connelly, Gene; Gallant, Paul L.
PATENT ASSIGNEE(S):       Cubist Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 74 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.          KIND  DATE          APPLICATION NO.   DATE
     ----------------    ----  --------      ---------------   --------
     WO 9935494           A1   19990715      WO 1999-US474     19990108
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9922181           A1   19990726      AU 1999-22181     19990108
     EP 1046034           A1   20001025      EP 1999-902132    19990108
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     NO 2000003515        A    20000907      NO 2000-3515      20000707
PRIORITY APPLN. INFO.:                      US 1998-70965     19980109
                                            US 1998-76638     19980303
                                            US 1998-81753     19980414
                                            US 1998-85844     19980518
                                            US 1998-89828     19980619
                                            US 1998-94698     19980730
                                            US 1998-100211    19980914
                                            US 1998-101718    19980924
                                            US 1998-107751    19981110
```

AB The invention comprises methods useful within a larger process for identifying compds. and/or designing further compds. with activity to produce a desired phenotype (for example, growth inhibition) in cells whose target cell component is the subject of certain studies to identify such compds. The invention employs constructed cells comprising a regulable gene encoding a biomol. which modulates (inhibits or activates) in vivo the function of a target component of the cell which can be an enzyme for example. The process incorporates methods for identifying biomols. that bind to a chosen target cell component in vitro, methods for identifying biomols. that also bind to the chosen target and modulate its function intracellularly, causing a phenotypic effect. The intracellular effect of a biomol. can be tested in cell culture, or tested after **introduction** of the constructed cells into a host **mammal** in vivo, and methods for identifying compds. that compete with the biomols. for sites on the target in competitive binding assays. Compds. identified by the series of steps in this process are candidates for drugs with the desired activity on the cell. Targets for which such compds. can be identified are validated as being essential to a phenotype of the cell.

REFERENCE COUNT: 2

REFERENCE(S): (1) Upjohn Co; WO 9117260 A 1991 CAPLUS
(2) Zeneca Ltd; GB 2303209 A 1997 CAPLUS

=> D HIS

(FILE 'HOME' ENTERED AT 18:27:20 ON 09 MAR 2001)

FILE 'MEDLINE, EMBASE, CAPLUS, BIOSIS' ENTERED AT 18:27:40 ON 09 MAR 2001

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L1          485 S (TALLY, F?)/IN,AU
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L3           58 S (WENDLER, P?)/IN,AU
L4          108 S (CONNELLY, G?)/IN,AU
L5           72 S (GALLANT, C?)/IN,AU
L6          492 S (GALLANT, D?)/IN,AU
L7            0 S L1 AND L2 AND L3 AND L4 AND L6
L8         1977 S L1 OR L2 OR L3 OR L4 OR L6
L9           14 S L8 AND TET
L10           6 DUPLICATE REMOVE L9 (8 DUPLICATES REMOVED)
L11          15 S L8 AND (METHOD (S) (ISOLATION OR IDENTIFICATION OR SCREENING
L12          11 DUPLICATE REMOVE L11 (4 DUPLICATES REMOVED)
L13           0 S L8 AND PRO3
L14           0 S L8 AND PC3844
L15           0 S L8 AND PRORS
L16           1 S L8 AND (INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANI
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=> S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?) AND (INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANISM))

UNMATCHED LEFT PARENTHESIS '((DRUG'
The number of right parentheses in a query must be equal to the number of left parentheses.

=> S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?)) AND (INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANISM))

2 FILES SEARCHED...

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L17         597 ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?)) AND
                (INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANISM))
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=> S L17 AND TET

L18 0 L17 AND [redacted]ET

=> S L17 AND INDUC?

L19 126 L17 AND INDUC?

=> S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?)) AND ((DNA OR VECTOR) (S)INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANISM))

2 FILES SEARCHED...
L20 75 ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?)) AND ((DNA OR VECTOR) (S) INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL
OR ORGANISM))

=> S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?)) AND ((RECOMBINANT (2N) CELL) (S)INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANISM))

2 FILES SEARCHED...
L21 0 ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?)) AND ((RECOMBINANT (2N) CELL) (S) INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANISM))

=> S L20 AND (EX (2W) VIVO)

L22 7 L20 AND (EX (2W) VIVO)

=> D TI L22 1-7

L22 ANSWER 1 OF 7 MEDLINE
TI Naked DNA and adenoviral immunizations for immunotherapy of prostate cancer: a phase I/II clinical trial.

L22 ANSWER 2 OF 7 MEDLINE
TI Molecular therapy for renal diseases.

L22 ANSWER 3 OF 7 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Naked DNA and adenoviral immunizations for immunotherapy of prostate cancer: A phase I/II clinical trial.

L22 ANSWER 4 OF 7 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Prostate cancer immunotherapy at the dawn of the new millennium.

L22 ANSWER 5 OF 7 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Molecular therapy for renal diseases.

L22 ANSWER 6 OF 7 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI The biotechnology of gene therapy.

L22 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2001 BIOSIS
TI Naked DNA and adenoviral immunizations for immunotherapy of prostate cancer: A phase I/II clinical trial.

=> D IBIB AB L22 1, 2, 4, 6

L22 ANSWER 1 OF 7 MEDLINE
ACCESSION NUMBER: 2000436262 MEDLINE
DOCUMENT NUMBER: 20355043
TITLE: Naked DNA and adenoviral immunizations for immunotherapy of
prostate cancer: a phase I/II clinical trial.

AUTHOR: Mi[redacted]heff M; Tchakarov S; Zoubak S; L[redacted]ukinov D; Botev C; Al[redacted]nkova I; Georgiev G; Petrov S; L[redacted]yman H T
CORPORATE SOURCE: American Foundation for Biological Research, Rockville, MD 20852, USA.. mincheffm@netscape.net
SOURCE: EUROPEAN UROLOGY, (2000 Aug) 38 (2) 208-17.
Journal code: ENM. ISSN: 0302-2838.
PUB. COUNTRY: Switzerland
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY WEEK: 20001104

AB **INTRODUCTION** AND OBJECTIVES: **Animal** studies have indicated that the use of syngeneic dendritic cells that have been transfected **ex vivo** with **DNA** for tumor-specific antigen results in tumor regression and decreased number of metastases. Additional studies have also suggested the possibility to modulate the dendritic cells in vivo either by 'naked' **DNA** immunization or by injecting replication-deficient viral vectors that carry the tumor-specific **DNA**. Using the prostate- specific membrane antigen (PSMA) as a **target** molecule, we have initiated a clinical trial for immunotherapy of prostate cancer. The primary objective of the study was to **determine** the safety of the PSMA vaccine after repeated intradermal injections. METHODS: We have included the extracellular human PSMA **DNA** as well as the human CD86 **DNA** into separate expression vectors (PSMA and CD86 plasmids), and into a combined PSMA/CD86 plasmid. In addition, the expression cassette from the PSMA plasmid was inserted into a replication deficient adenoviral expression **vector**. Twenty-six patients with prostate cancer were entered into a phase I/II toxicity-dose escalation study, which was initiated in spring 1998. Immunizations were performed intradermally at weekly intervals. Doses of **DNA** between 100 and 800 &mgr;g and of recombinant virus at 5x10(8) PFUs per application were used. RESULTS AND CONCLUSION: No immediate or long-term side effects following immunizations have been recorded. All patients who received initial inoculation with the viral **vector** followed by PSMA plasmid boosts showed signs of immunization as evidenced by the development of a delayed-type hypersensitivity reaction after the PSMA plasmid injection. In contrast, of the patients who received a PSMA plasmid and CD86 plasmid, only 50% showed signs of successful immunization. Of the patients who received PSMA plasmid and soluble GM-CSF, 67% were immunized. However, all patients who received the PSMA/CD86 plasmid and sGM-CSF became immunized. The patients who did not immunize during the first round were later successfully immunized after a boost with the viral **vector**. The heterogeneity of the medical status and the presence in many patients of concomitant hormone therapy does not permit unequivocal interpretation of the data with respect to the effectiveness of the therapy. However, several responders, as evidenced by a change in the local disease, distant metastases, and PSA levels, can be **identified**. A phase II clinical study to evaluate the effectiveness of the therapy is currently underway.

L22 ANSWER 2 OF 7 MEDLINE
ACCESSION NUMBER: 96438576 MEDLINE
DOCUMENT NUMBER: 96438576
TITLE: Molecular therapy for renal diseases.
AUTHOR: Lipkowitz M S; Klotman M E; Bruggeman L A; Nicklin P; Hanss

B; [redacted]ppaport J; Klotman P E
CORPORATE SOURCE: De[redacted]tment of Medicine, Mount Sinai [redacted]hool of Medicine, New
York, NY 10029, USA.
SOURCE: AMERICAN JOURNAL OF KIDNEY DISEASES, (1996 Oct) 28 (4) 475-92. Ref: 169
Journal code: 3H5. ISSN: 0272-6386.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY WEEK: 19970104

AB The **introduction** of molecular therapy through the delivery of nucleic acids either as oligonucleotides or genetic constructs holds enormous promise for the treatment of renal disease. Significant barriers remain, however, before successful organ-specific molecular therapy can be applied to the kidney. These include the development of methods to **target** the kidney selectively, the definition of vectors that transduce renal tissue, the **identification** of appropriate molecular targets, the development of constructs that are regulated and expressed for long periods of time, the demonstration of efficacy in vivo, and the demonstration of safety in humans. As the genetic and pathophysiologic basis of renal disease is clarified, obvious targets for therapy will be defined, for example, polycystin in polycystic kidney disease, human immunodeficiency virus (HIV) type 1 in HIV-associated nephropathy, alpha-galactosidase A in Fabry's disease, insulin in diabetic nephropathy, and the "minor" collagen IV chains in Alport's syndrome. In addition, several potential mediators of progressive renal disease may be amenable to molecular therapeutic strategies, such as interleukin-6, basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF), and transforming growth factor-beta(TGF-beta). To test the in vivo efficacy of molecular therapy, appropriate **animal** models for these disease states must be developed, an area that has received too little attention. For the successful delivery of genetic constructs to the kidney, both viral and nonviral **vector** systems will be required. The kidney has a major advantage over other solid organs since it is accessible by many routes, including intrarenal artery infusion, retrograde delivery through the uroexcretory pathways, and **ex vivo** during transplantation. To further restrict expression to the kidney, tropic vectors and tissue-specific promoters also must be developed. For the purpose of inhibition of endogenous or exogenous genes, current therapeutic modalities include the delivery of antisense oligodeoxynucleotides or ribozymes. For these approaches to succeed, we must gain a much better understanding of the nature of their transport into the kidney, requirements for specificity, and in vivo mechanisms of action. The danger of a rush to clinical application is that superficial approaches to these issues will likely fail and enthusiasm will be lost for an area that should be one of the most exciting developments in therapeutics in the next decade.

L22 ANSWER 4 OF 7 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000197685 EMBASE
TITLE: Prostate cancer immunotherapy at the dawn of the new millennium.
AUTHOR: Salgaller M.L.
CORPORATE SOURCE: M.L. Salgaller, Northwest Biotherapeutics, Inc., 2203 Airport Way South, Seattle, WA 98134, United States.

ml[redacted]nwbio.com
SOURCE: Ex[redacted]t Opinion on Investigational D[redacted]s, (2000) 9/6 (1217-1229).
Refs: 108
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Standard treatments for adenocarcinoma of the prostate, such as surgery, hormones, radiation and chemotherapy, often achieve a clinical response, but this is usually short-lived. Prostate cancer frequently recurs and second-line therapies have a poor response rate. Many clinicians seem comfortable in limiting their philosophy of treating advanced recurrent disease merely to new regimens of failed therapies, such as combination chemotherapy. However, other medical researchers have chosen to pursue novel approaches, including immunotherapy, several of which are summarised in this review. Although ranging widely in antigen specificity, all attempt to exploit the body's natural antitumour immunity. Furthermore, all aim to stimulate immunity above a threshold level necessary for tumour regression or to induce stability in the face of progression. The goal of in vivo or **ex vivo** gene therapy is the modification of gene expression within an antigen-presented cell by the **introduction** of a **vector**, **DNA**, or RNA. Within that field, much progress has been made and is ongoing currently concerning gene delivery systems, **target identification** and characterisation. Comparatively, monoclonal antibodies are an established type of cancer immunotherapy. However, the more recent development of humanised or fully human antibodies, as well as novel moieties they can be coupled to, renews their prospects for clinical impact. Lastly, various cell-based therapies are the focus of several recent clinical studies demonstrating tumour regression or stabilisation. Immune cells, for example, T-lymphocytes and dendritic cells, have already demonstrated treatment benefit, as well as the ability to maintain an excellent quality of life for participants. Overall, there is a multitude of approaches being considered for the treatment of prostate cancer. The following review concentrates on those approaches that are currently in human or **animal** studies and have a specific emphasis on prostate cancer.

L22 ANSWER 6 OF 7 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96251000 EMBASE
DOCUMENT NUMBER: 1996251000
TITLE: The biotechnology of gene therapy.
AUTHOR: Pappas M.G.
CORPORATE SOURCE: Advanced Instruments, Inc., Two Technology Way,Norwood, MA 02062, United States
SOURCE: Drug Development and Industrial Pharmacy, (1996) 22/8 (791-803).
ISSN: 0363-9045 CODEN: DDIPD8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
016 Cancer
022 Human Genetics

02[redacted] Clinical Biochemistry
LANGUAGE: En[redacted]sh
SUMMARY LANGUAGE: English
AB The prospect for correcting highly morbid or fatal inherited diseases, or ameliorating cancer and acquired, deadly infectious diseases such as AIDS using gene therapy is very exciting. Numerous recent advances in molecular biology make it possible, not only to **identify** and locate genes associated with human inherited disorders and cancers, but to potentially correct these disorders with functional genes. These advances include more rapid gene **identification**, isolation and sequencing techniques, a better understanding of the functions and relationships between genes and their products in vivo, the development and study of human and model **organism** genomes, elucidation of genetic disease pathology using **animal** genetic disease models, advanced computer amino acid and nucleotide sequencing software and data bases, and the development and use of novel chemical, physical, and viral **vector** gene delivery methods. Functional genes are **introduced** using two approaches, **ex vivo** and in vivo gene therapy. In **ex vivo** therapy, autologous cells are removed from the patient, genetically altered by inserting the functional gene, characterized, and then returned to the patient; in in vivo therapy, functional genes are packaged for delivery directly into the patient, where cellular uptake and gene expression occurs. Scores of clinical trials have been federally approved to treat patients with a variety of inherited disorders, cancers, and acquired diseases using these two approaches. Roadblocks to long-lasting gene therapy include understanding more completely the biological functions of somatic cells or organs targeted for gene therapy, targeting appropriate host cells and achieving high gene delivery rates in these cells, regulating and sustaining gene expression through optimal **DNA** insertion into chromosomes such that other cellular functions are not adversely affected, and the prevention of **vector**-induced diseases or cancers. Ethical considerations regarding proper use of somatic gene therapy and the potential for germline gene therapy must also be seriously considered. The prospect of permanent correction of highly morbid or fatal maladies using gene therapy could prove to be one of the great advances in public health and could revolutionize the **identification** and gene-**drug** treatment of a broad spectrum of inherited and acquired human diseases.

=> D HIS

(FILE 'HOME' ENTERED AT 18:27:20 ON 09 MAR 2001)

FILE 'MEDLINE, EMBASE, CAPLUS, BIOSIS' ENTERED AT 18:27:40 ON 09 MAR 2001

| | | | |
|---|---|---|---|
| L1 | 485 | S | (TALLY, F?)/IN,AU |
| L2 | 855 | S | (TAO, J?)/IN,AU |
| L3 | 58 | S | (WENDLER, P?)/IN,AU |
| L4 | 108 | S | (CONNELLY, G?)/IN,AU |
| L5 | 72 | S | (GALLANT, C?)/IN,AU |
| L6 | 492 | S | (GALLANT, D?)/IN,AU |
| L7 | 0 | S | L1 AND L2 AND L3 AND L4 AND L6 |
| L8 | 1977 | S | L1 OR L2 OR L3 OR L4 OR L6 |
| L9 | 14 | S | L8 AND TET |
| L10 | 6 | | DUPLICATE REMOVE L9 (8 DUPLICATES REMOVED) |
| L11 | 15 | S | L8 AND (METHOD (S) (ISOLATION OR IDENTIFICATION OR SCREENING |
| L12 | 11 | | DUPLICATE REMOVE L11 (4 DUPLICATES REMOVED) |

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L13             0 S L8 AND PRO3
L14             0 S L8 AND PC3844
L15             0 S L8 AND PRORS
L16             1 S L8 AND (INTRODUC? (S) (SUBJECT OR MAMMAL OR ANIMAL OR ORGANI
L17           597 S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?))
AND
L18             0 S L17 AND TET
L19           126 S L17 AND INDUC?
L20            75 S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?))
AND
L21             0 S ((DRUG OR TARGET) (S) (IDENTIF? OR SCREEN? OR DETERMIN?))
AND
L22             7 S L20 AND (EX (2W) VIVO)
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Attach paper #15

EAST: DERWENT EPO JPO USPAT 3/11/01 09/227,687

| | | |
|---|---|---|
| L1 | 12 | tally-f$.in. |
| L2 | 119 | tao-j$.in. |
| L3 | 32 | wendler-p$.in. |
| L4 | 11 | connelly-g$.in. |
| L5 | 78 | gallant-d$.in. |
| L6 | 154 | shen-x$.in. |
| L7 | 1820 | zhang-j$.in. |
| L8 | 2211 | 1 or 2 or 3 or 4 or 5 or 6 or 7 |
| L9 | 7 | 8 and aureus |
| L10 | 133 | methionyl$ and aureus |
| L11 | 9 | (methionyl$ with synthetase) and aureus |
| L12 | 1069 | pathogen and (method with (screening or identifying or isolating or determining) with (compound or target or inhibitor)) |
| L13 | 313 | 12 and aureus |
| L14 | 4 | 13 and (methionyl$ with synthetase) |
| L15 | 327 | pathogen and (method with (screening or identifying or isolating or determining) with (compound or target) with inhibit$) |
| L16 | 0 | 15 and (in adj2 vivo) |
| L17 | 5 | 15 and (test adj3 animal) |
| L18 | 10 | pathogen and (method with (screening or identifying or isolating or determining) with (compound or target) with inhibit$) with animal |
| L19 | 10 | pathogen and (method with (screening or identifying or isolating or determining) with (compound or target) with inhibit$ with animal) |
| L20 | 10 | 18 or 19 |
| L21 | 109 | pathogen and (method with (screening or identifying or isolating or determining) with (compound or target) with inhibit$) and aureus |
| L22 | 159 | pathogen and ( (screening or identifying or isolating or determining) with (compound or target) with inhibit$) and aureus |
| L23 | 16 | pathogen and ( (screening or identifying or isolating or determining) with (compound or target) with inhibit$ with animal) and aureus |
| L24 | 309 | pathogen and ( (screening or identifying or isolating or determining) with (compound or target) with inhibit$) and (animal with (introduc$ or infect$)) |
| L25 | 235 | pathogen and ( (screening or identifying or isolating or determining) with (compound or target) with inhibit$) and (animal with (introduc$ or infect$) with (cell or pathogen)) |
| L26 | 84 | pathogen and ( (screening or identifying or isolating or determining) with (compound or target) with inhibit$) and (animal with (introduc$ or infect$) with (cell or pathogen)) and aureus |
| L27 | 0 | pathogen and ( (screening or identifying or isolating or determining) with (compound or target) with inhibit$ with animal with (introduc$ or infect$) with (cell or pathogen)) and aureus |